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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 10/588,687 | 07/18/2007 | David C. S. Huang | 007193-24 US | 9234 |
| 36234 7590 09/15/2009 THE MCCALLUM LAW FIRM, P. C. 685 BRIGGS STREET PO BOX 929 ERIE, CO 80516 | | | | |
| EXAMINER | | | | |
| GUCKER, STEPHEN | | | | |
| ART UNIT | | PAPER NUMBER | | |
| 1649 | | | | |
| MAIL DATE | | DELIVERY MODE | | |
| 09/15/2009 | | PAPER | | |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/588,687

Applicant(s)

HUANG ET AL.

Examiner

STEPHEN GUCKER

Art Unit

1649

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 July 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 19-38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 19-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SF/ICE)
Paper No(s)/Mail Date 3/8/07
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

1. Claim 18 is objected to because of the following informalities: it is numbered as claim 18. It has been renumbered as claim 38.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 19-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the invention and Breadth of the claims: The claims are directed to methods of generating an antagonist of the Bcl-2 family of proteins by selecting a scaffold BH3-only protein structure with residue positions defining an amphipathic α -helix formed by the BH3

domain; selecting one or more residues positions associated with a promiscuous binding phenotype of a BH3-only protein; substituting amino acid residues conferring a promiscuous phenotype for a molecule selected from the group consisting of amino acids and amino acid chemical analogs which confer a restrictive binding pattern to a Bcl-2 protein; and analyzing the interaction of each substitution for an ability to induce a more restrictive spectrum of binding to a Bcl-2 protein. In addition, the claims encompass computational methods, a computer program product and an apparatus for achieving the aforementioned goal of designing an antagonist, and methods of treating and preventing cancer. The breadth of the claims are exceedingly wide, encompassing every manner of screening both actual and by computer simulation, followed by the claimed generation of the antagonist product (which the aforementioned screening may or may not provide guidance or direction for) by every means possible, followed by the treatment and prevention of every cancer. Furthermore, the nature of the invention is extremely unpredictable and not routine, as the ability to predict and simulate protein structure and activity is poor, the ability to generate useful antagonists poorer still, and the treatment and prevention of cancer by these methods has never been demonstrated.

Thus, the nature of the invention and the breadth of the claims renders the invention unpredictable and not adequately supported by the disclosure or the prior art.

State of the prior art and level of predictability in the art: The art provides insufficient guidance with respect to routine experimentation with a reasonable expectation of success to enable the claims.

Thus, the art relevant to actually generating antagonists of the instant invention is undeveloped, and since it is a complex biological system with many competing interactions, the invention is innately unpredictable as well.

Amount of direction provided by the inventor and existence of working examples: There are no working examples. What direction and guidance exists in the disclosure is drawn to a narrow subset of a single species of protein that was mutated in one small domain that would require undue experimentation to work with in order to support the breadth of the claims for every and all unrelated proteins, domains, methods of treatment, generating antagonists, etc. because it is not representative of the characteristics of the extremely broad genres recited. No antagonist was generated, no computer system or apparatus developed, and no clinical treatments of any kind were performed or even attempted.

Thus, the disclosure provides no validation for the prophetic inventions described.

Relative skill of those in the art and quantity of experimentation needed to make or use the invention: Although the relative level of skill in the art is high, the skilled artisan would not be able to make and use the invention as asserted in the application without undue experimentation to generate the antagonists by any methods and the computer systems and apparatus and methods of treatment as claimed.

Given this high degree of unpredictability and the absence of any evidence to indicate that the methods of the instant invention are effective in treating or preventing any cancer or even of generating a single antagonist the claims represent no more than a theoretical possibility. This is not sufficient to meet the enablement requirement of 35 USC §112, first paragraph.

In view of the foregoing, using the invention as contemplated in the specification would require undue experimentation. Therefore, the claims are properly rejected under 35 USC §112, first paragraph, as lacking an enabling disclosure.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 19-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The "generating of the antagonist" limitation of the preamble is not reflected in the body of the claims, rendering the claims vague and indefinite. Furthermore, many of the various terms and phrases in the claims are not adequately defined as to their actual process steps or their meets and bounds. These would include "selecting a scaffold," "promiscuous binding phenotype," "BH3-only protein," "analyzing the interaction," "more restrictive spectrum," "determining the conformation," "generating a chemical compound which mimics said scaffold and conformational part conferring a restrictive spectrum," "selecting a collection," "providing a sequence alignment...and comparing said sequence alignment," "creating a scoring function," "using said scoring function and at least one additional scoring function," "conformational equivalents of optimized protein sequences," "the contribution to tertiary structure the residue makes in the BH3-only protein," "code that adds said SF to provide a sum corresponding to a Pv," and "provide a sum of said SF corresponding to a Pv for said compound."
6. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claim 38 provides for the use of an antagonist, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 38 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is 571-272-0883. The examiner can normally be reached on Mondays through Fridays from 0930 to 1800.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

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system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/S. G./

Examiner, Art Unit 1649

Stephen Gucker

September 15, 2009

/Jeffrey Stucker/

Supervisory Patent Examiner, Art Unit 1649